

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



542602

(43) International Publication Date  
5 August 2004 (05.08.2004)

PCT

(10) International Publication Number  
**WO 2004/064838 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 31/4535**

(21) International Application Number:  
PCT/CA2004/000033

(22) International Filing Date: 19 January 2004 (19.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
2416799 17 January 2003 (17.01.2003) CA  
60/460,397 7 April 2003 (07.04.2003) US

(71) Applicant (for all designated States except US): **UNIVERSITY HEALTH NETWORK [CA/CA]**; 700 University Avenue, 8th Floor, Toronto, Ontario M5G 1X6 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BERGER, Stuart, A.** [CA/CA]; 220 Strathearn Road, Toronto, Ontario M6C 1S4 (CA). **ZHANG, Yicheng** [CA/CA]; 19B Sullivan Street, Toronto, Ontario M5B 1B8 (CA).

(74) Agent: **BERESKIN & PARR**; 40 King Street West, 40th Floor, Toronto, Ontario M5H 3Y2 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **PHARMACEUTICAL COMPOSITIONS AND METHODS FOR TREATING MULTIDRUG RESISTANT CANCER**

(57) Abstract: The invention relates to a pharmaceutical composition comprising i) ketotifen or an analog thereof and ii) a chemotherapeutic drug subject to multi-drug resistance by P-gp, such as doxorubicin or an analog thereof. The pharmaceutical composition is useful for treating cancer. The pharmaceutical composition is also useful for i) preventing or treating multi-drug resistance in a subject or ii) preventing a chemotherapeutic drug subject to multi-drug resistance by P-gp induced cardiac tissue damage in a subject, such as doxorubicin or an analog thereof. The invention relates to a pharmaceutical composition comprising i) ketotifen or an analog thereof and ii) a chemotherapeutic drug subject to multi-drug resistance by P-gp, such as doxorubicin or an analog thereof. The pharmaceutical composition is useful for treating cancer. The pharmaceutical composition is also useful for i) preventing or treating multi-drug resistance in a subject or ii) preventing a chemotherapeutic drug subject to multi-drug resistance by P-gp induced cardiac tissue damage in a subject, such as doxorubicin or an analog thereof.



**WO 2004/064838 A1**